SYNTHESIS OF DRIM-8-EN-7-ONE

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A mixture of bicyclohomofarnesenic esters (0.1 g) was oxidized in boiling acetic acid with 0.164 g of $K_2Cr_2O_7$ for 12 h. By preparative TLC on SiO_2, the reaction product yielded 0.04 g (38%) of an ester (IV) of 7-oxobicyclohomofarnes-8-enic acid (V), mp 99-100.5°C (from light petroleum ether), $[\alpha]_D^{21}$ + 124.3° ($CHCl_3$); $\lambda_{max}^{ethanol}$ 248 nm (log ε 3.75). Then 0.18 g of (IV) was boiled with a solution of 0.75 g of KOH in 6.5 ml of ethanol for 3 h. After working up, 0.14 g (9.3%) of drim-8-en-7-one was obtained with mp 51-52°C, $[\alpha]_D^{25}$ + 86° ($CHCl_3$); $\lambda_{max}^{ethanol}$ 249.5 (log ε 4.14). Characteristics of its IR and NMR spectra are given.

The sesquiterpene ketone drim-8-en-7-one (I) was isolated by Swedish chemists [1] from Greek tobacco, where it is present in trace amounts. They performed its nine-stage synthesis starting from drimenol. It was reported that the ketone (I) was odorless. Later, drim-8-en-7-one (I) was detected among the products of the oxidation of the diterpenoid sclareol [2] and it was found that it actually possesses a strong ambergris-like odor [3] and may be of interest for the perfumery industry. In view of this, we have perfected a three-stage synthesis of drim-8-en-7-one (I) from the readily accessible bicyclohomofarnesane lactone norambreinolide (II).

By a known method [4], norambreinolide (II) was converted into a mixture of isomeric bicyclohomofarnesenic esters (III), which were oxidized with potassium dichromate to the α,β-unsaturated oxo ester (IV). As is well known, the allyl oxidation of unsaturated compounds can be effected by such reagents as chromium trioxide in acetic acid [5, 6], tertiary butyl chromate [5, 7, 8], a complex of chromium trioxide with pyridine [9, 10], N-bromosuccinimide [11], pyridine chlorochromate [12], and selenium dioxide [5, 13]. However, when the mixture of esters (III) was oxidized with these reagents, complex mixtures of substances were formed and the yield of the oxo ester (IV) was low. The best results were obtained when the mixture of esters (III) was oxidized with potassium dichromate [13], although in this case, as well, the reaction product consisted of a mixture of substances and the maximum yield of the oxo ester (IV) was only 41.5%. This was achieved by performing the oxidation in boiling acetic acid at a molar ratio of the mixture of esters (III) and the oxidant of 1:0.74 for 12 h. With a longer reaction time the oxo ester (IV) first formed underwent further oxidation and its yield fell.

The oxo ester (IV) was isolated from the reaction products by preparative TLC on silica gel. Its structure was shown on the basis of spectral characteristics. The IR spectrum of (IV) contained the absorption bands of an ester group at 1750 cm^{-1} and of a conjugated carbonyl at 1627 and 1680 cm^{-1}. The presence of the latter was confirmed by the UV spectrum, which had a maximum at 248 nm showing the conjugation of the keto group with a tetrasubstituted double bond. The PMR spectrum of the oxo ester (IV) showed the signals of three methyl groups at quaternary carbon atoms (0.95 and 1.07 ppm, singlets, 6 H and 3 H, respectively); of one methyl group at C_8 (1.68, singlet, 3 H); of a methylene group at C_{11} (3.24 ppm, singlet, 2 H); and of a methoxy group (3.73 ppm, singlet, 3 H). The observed downfield shift of the methyl group at C_{10} confirmed the presence of a double bond in the C_8—C_9 position, descreening the protons of this group.

The saponification of the oxo ester (IV) formed the oxo acid (V), which decarboxylated spontaneously and gave an almost quantitative yield of drim-8-en-7-one (I), the properties

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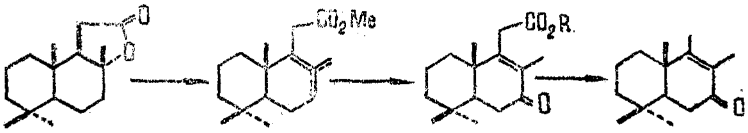
of which were identical with those described by Aasen et al. [1].



II III IV. R = CH_3 V. R = H I

Norambreinolide (II) is also, apparently, a precursor of the ketone (I) in tobacco in which, as is well known [14], it is present.

EXPERIMENTAL

IR spectra were taken on UR-20 and Specord-71 IR spectrophotometers in CCl_4, UV spectra on a Specord UV-Vis spectrometer in ethanol, and NMR spectra on a RS-60 instrument in CCl_4 (δ, TMS). Angles of optical rotation were measured on a Polamat S instrument. The melting points of the substances were determined on a Boëtius heated stage. GLC analysis was carried out on a Chrom-4 chromatograph with a FID using glass columns with dimensions of 2 × 3.5 mm filled with XE-60 (5% on Chromaton N-AW-DMCS with programming of the temperature from 130 to 200°C at a rate of heating of 3 deg/min, the carrier gas being He (60 ml/min), and the temperature of the evaporator 200°C.

The Oxo Ester (IV). A solution of 0.1 g of the liquid mixture of esters (III) [4] in 2 ml of glacial acetic acid was treated with 0.164 g of finely ground potassium dichromate and the mixture was boiled under reflux for 12 h, after which it was cooled and diluted with water. The reaction products were extracted with ether and the extract was washed with water, with saturated sodium bicarbonate solution, and again with water and was dried with anhydrous sodium sulfate. After the solvent had been distilled off, the residue (0.095 g) was separated by preparative TLC on silica gel with a luminophore in the benzene–petroleum ether–ethyl acetate (90:10:5) system. The zone with R_f 0.43 was collected and the substance was eluted with ether. This gave 0.03 g of (IV), composition $C_{17}H_{26}O_3$ (yield 38%; according to GLC analysis, its yield was 41.5%). mp 99-100.5°C, $[\alpha]_D^{21}$ + 124.3° (c 2.6; $CHCl_3$).

Drim-8-en-7-one (I). The oxo ester (IV) (0.18 g) was boiled with a solution of 0.75 g of caustic potash in 6.5 ml of ethanol under reflux for 3 h. Then the reaction mixture was diluted with water, acidified with hydrochloric acid, and extracted with ether. After the usual working up and distillation of the solvent, the residue was recrystallized from light petroleum ether. This gave 0.14 g (98.3%) of the ketone (I), mp 51-52°C. $[\alpha]_D^{25}$ + 86 (c 4.0; $CHCl_3$). IR spectrum (cm^{-1}): 1375, 1390 (gem-dimethyl groups); 1610, 1660 (α,β-unsaturated ketone). UV spectrum (nm): λ_{max} 249.5 (log ε 4.14). According to the literature [1]: mp 52-53°C; $[\alpha]_D$ + 58.7° ($CHCl_3$). A direct comparison of the physicochemical constants of the products obtained and a sample of the ketone (I) showed that they were identical.

SUMMARY

The three-stage synthesis of drim-8-en-7-one from norambreinolide has been effected.

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OXIDATIVE TRANSFORMATIONS OF CEMBRANE DITERPENOIDS.

V. REACTION OF CEMBRENE WITH N-BROMOSUCCINIMIDE IN AQUEOUS ACETONE

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The reaction of the diterpene hydrocarbon cembrane with N-bromosuccinimide in aqueous acetone takes place as the addition of the elements of hypobromous acid, leading to products of addition at the C_4-double bond — 5R- and 5S-bromoisocembrols and 5R-bromo-4-epiisocembrol. At the same time, products of the bromination of cembrene — 18-and 5-bromocembrenes — are formed. The structures of the compounds obtained were shown with the aid of chemical transformations and spectral characteristics. Under the action of pyridine, the bromohydrins obtained underwent dehydrobromination with the formation of products having a rearranged cembrane skeleton. The stereochemistry of the cembrane bromohydrins is discussed in connection with the stereochemistry of known addition reactions to cembrane and the biogenesis of natural methyl ketones.

It has been shown previously that electrophilic addition to the double bonds of cembrane (I) takes place as a highly stereospecific process for epoxidations with peracids [1], for photooxidation [2], and for hydroxylation with potassium permanganate [3]. In order to synthesize new cembrane derivatives and to elucidate the stereochemistry of the addition of electrophilic particles of comparatively small volume to the cembrane molecule, we have investigated the products of the reaction of cembrene with N-bromosuccinimide in aqueous acetone. The reactions of olefins with this reagent in polar solvents take place as the addition of the elements of hypobromous acid [4]. Since the first stage of the reaction is an electrophilic attack by the bromonium ion, then, in addition to the normal products of addition to double bonds, cyclization products may be obtained. This is frequently observed in the case of such complex substrates as terpenoids, and the occurrence of cyclization may be considered as modeling biosynthetic transformations [5].

When the reaction was performed under the conditions usually used [4] with a molar ratio of cembrene and N-bromosuccinimide of 1:1.2, we obtained a mixture in which, in addition to unchanged cembrane, substances of hydrocarbon nature similar to cembrene, and highly polar compounds, there were three products with R_f 0.58, 0.47, and 0.36 (Silufol, using petroleum ether containing 20% of diethyl ether as the mobile phase). The product with R_f 0.58 was the main component of the reaction mixture. During ordinary column chromatography on silica gel, this compound decomposed, giving a mixture of substances the predominating component of which coincided according to TLC with the initial compound but

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